

Salivary alpha-amylase levels and hyperbolic discounting in male humans

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Abstract

OBJECTIVE: Little is known regarding the role of the sympathetic-adrenal-medullary (SAM) system in self-control and impulsivity in intertemporal choice (delay discounting), although the roles of dopaminergic and serotonergic systems have been extensively examined. This study was aimed to examine the relationships between salivary alpha-amylase (sAA, a non-invasive biological marker of adrenergic/SAM activities) levels and hyperbolic discounting, which is of interest in psychoneuroendocrinology and neuroeconomics. **METHODS:** We assessed degrees to which delayed monetary gains were discounted (hyperbolic discount rates) in healthy male students. Participants' sAA were also assessed. **RESULTS:** We observed negative relationships between sAA and hyperbolic discounting of small, medium, and large monetary gains. **CONCLUSIONS:** The results indicate that subjects with low sAA are impulsive in intertemporal choice. Implications for the roles of adrenergic and SAM systems in self-control in intertemporal choice are discussed.

Introduction

Impulsivity is a core deficit in neuropsychiatric disorders such as attention-deficit-hyperactivity disorders (ADHD), psychopathy, and addiction [1,2]. As such, neuropsychological functioning associated with impulsivity has attracted much attention [1,2,18]. In this study, we operationalized risky/impulsive behavior as a strong devaluation of delayed monetary gains, leading to a preference of small immediate rewards over large delayed ones (delay discounting of monetary gains), following a standard behavioral paradigm in neurobiochemical and neuroeconomic studies of impulsivity [2,3,4,6,7,8,9,11,12,17]. Impulsive psychiatric patients (e.g., drug addicts and

ADHDs) are reported to have stronger delay-discounting tendency than healthy controls [2,4,8,9].

Neuropharmacological investigations have demonstrated that monoamines (e.g., dopamine and serotonin) in the central nervous system and drug dependence-induced synaptic modifications in dopaminergic reward circuitry modulate delay discounting behavior [6,7,8,9]. Neuroeconomic studies employing fMRI have revealed that prefrontal and limbic reward-processing regions were activated during intertemporal choice [6,8]. We have also previously reported that severity of nicotine addiction is positively associated with the degree to which smokers discount delayed monetary gains, but not with the degree to which they discount uncertain rewards [9]. We have also conducted neuroendocrinological

studies on intertemporal choice and observed that low levels of cortisol (a stress hormone) and testosterone (a male hormone) are associated with rapid discounting of delayed monetary gains in men [11,12]. However, it is yet to be elucidated how adrenergic activities in the brain are associated with impulsivity and self-control in intertemporal choice, although this question is important for psychopharmacological treatments for impulsive neuro-psychiatrics such as ADHD and drug dependent patients.

Recent progress in non-invasive measurement of neuroendocrine and neuroactive substances in saliva has made it possible to measure salivary alpha-amylase (sAA) levels [15,16], which may reflect (nor)adrenergic and SAM (sympathetic-adrenal-medullary) activities [15,16]. It has been demonstrated that sAA elevation is one of the stress-response types which have pathways distinct from HPA (hypothalamic-pituitary-adrenal) axis [15,16]. Because much effort has been expended to investigate the relationships between impulsivity and HPA activities [5,11,14], it may now be important to examine the relationship between impulsivity and adrenergic/SAM activities in a more extensive manner, because, to date, little is known regarding the relationship between adrenergic/SAM activities and impulsivity/self-control in intertemporal choice.

In this study we therefore examined relationships between sAA levels (probably reflecting adrenergic/SAM activity [15,16]) and delay discounting of monetary gains (in other words, impulsivity in intertemporal choice) in healthy male students, by utilizing well-established Kirby's MCQ (monetary choice questionnaire) for the assessment of subjects' discounting rates [4,12].

Methods

Participants and saliva collection

A total of 18 healthy male students (age: 20.3 ± 2.81) participated in the present study. It should be noticed that, to avoid influences of chronic nicotine-induced neuroadaptation on discounting behavior [1,9], only non-smokers were included in the study. Further, subjects with physical or psychiatric illnesses were excluded. Each participant collected two saliva samples in the evenings (14:00–18:00). The participants were asked to refrain from the consumption of alcohol beginning from the night before the samples were collected and, as far as possible, to obtain sufficient sleep. They were also instructed to maintain an interval of 6 h after brushing their teeth, at least 1 h after eating or drinking any fluid other than water, and 30 min after any strenuous exercise while collecting the samples of saliva. The detailed methodology of sAA measurement is denoted below. The participants also answered Kirby's questionnaire (explained below [4]) for the assessment of their discounting rates of delayed gains, and received a nominal amount of money (1,000 yen). This study was approved by the ethical committee on the use of human subjects at the Graduate School of Arts and Sciences, the University of Tokyo.

Materials

Kirby's MCQ (monetary choice questionnaire)

We adopted the same procedure for assessing subject's discount rates as previous neuroendocrinological and neuroimaging studies of intertemporal choice [8,12]. Studies in neuropsychopharmacology, psychoneuroendocrinology, and behavioral neuroeconomics have repeatedly observed that human and animal subject's delay discounting is well described by the hyperbolic discount function [2,3,4,7,8,9,12,13]:

$$V(D) = 1/(1+kD) \quad (\text{equation 1})$$

where $V(D)$ is a subjective value of delayed rewards at delay time D , and k (a hyperbolic discount rate) is a free parameter indicating subject's impulsivity in intertemporal choice (larger k values correspond to more rapid/steeper discounting; while smaller k values indicate self-control in intertemporal choice). In order to assess subject's discount rate k , as defined in equation 1, Kirby's MCQ [4,12] was used. Kirby's MCQ consists of 27 questions relating to a choice between smaller immediate rewards and larger but delayed rewards (e.g. "Would you prefer 54 dollars today or 55 dollars in 117 days?"). According to the standard analysis procedure of MCQ, established by Kirby and colleagues [4], we calculated subjects' discounting rates (i.e. k s) of three different sizes (small, medium, and large) of monetary gains. A total of three discount rates (i.e., small, medium, and large gains) were obtained for each subject. Geometric-mean discounting rates for different sizes were calculated, following Kirby's procedure [4]. We then examined relationships between the hyperbolic discount rates of gains and sAA levels. In our Kirby MCQ form, all gains were expressed in terms of Japanese yen, with an exchange rate of one dollar to 100 yen. Because the distribution of the discount rate k is known to be skewed, we used logged k in the following analysis, according to a standard analytical procedure [4].

Salivary alpha-amylase (sAA) assay

For measuring SAM system activity, we employed the same methodology as Yamaguchi et al's investigation into the relationships between sAA and driver's fatigue with a commercial hand-held monitor of sympathetic nervous system indicated as sAA levels [16]. This monitor (cocoro meter, Nipro Co. Ltd, Japan), being sold for personal assessment of psychosocial stress levels, utilizes a reagent paper containing 2-chloro-4-nitrophenyl-4-O-beta-D-galactopyranosylmaltoside (Gal-G2-CNP), a substrate for amylase. When Gal-G2-CNP is hydrolyzed by amylase, the hydrolyzed product (CNP) changes emission wavelengths (reflectance) with time. The collecting paper was directly inserted into an oral cavity, and approximately 20–30 microl of saliva was collected from under the tongue within 10–30 s. Thus, the reflectance 30 s after the initial time was automatically measured by the optical device. A total of one minute was enough to measure the salivary amylase

activity. We have measured sAA levels twice in this manner and averaged sAA levels were defined as subject's resting sAA levels. Because sAA levels (measured with the monitor) over 61 kU/L is the maximal stress reaction level (too high sAA as resting levels), we have removed two subjects with sAA higher than 61 kU/L. It is noteworthy here that inclusion of these subjects did not essential alter the following results when Spearman's rank correlation analysis was utilized in order to exclude the influences of outliers.

Data analysis and statistical procedure

Following Kirby's procedure [4], the logged discount rates of gains were calculated as denoted above. We then conducted Pearson's product-moment correlation analysis between sAA and logged discount rates (note that Spearman's rank correlation analysis also revealed the same statistical result). Data are expressed in terms of Mean \pm SD. Significance level is set at 0.05 throughout.

Results

Characteristics of salivary alpha-amylase (sAA) level and discount rate

Subjects' sAA level was 30.5 ± 11.4 kU/L. This range of sAA is similar to values reported previously in studies employing the same methodology of sAA assessment [16].

The hyperbolic discount rates (i.e., k s in equation 1) of small, medium, large gains were 0.031305169 ± 0.0521 ,

0.01651153 ± 0.0211 , and 0.011560697 ± 0.01685 respectively ($N=16$). We observed that smaller rewards were more steeply discounted (the magnitude effect on discounting), as indicated as larger discount rates for smaller reward sizes ($p < 0.05$). The discount rate averaged over three reward sizes was 0.017497 ± 0.02505 ($N=16$). These discount rate values are similar to values reported in previous studies [4,12].

Relationship between salivary alpha-amylase (sAA) level and discount rate

Pearson's correlation analysis showed significant negative correlations ($N=16$, $p < 0.05$) between sAA, and the logged discount rates for gains of all sizes ($r = -0.51$, -0.49 , -0.59 , for small, medium, and large rewards, respectively, $p < 0.05$, Figure 1A–C); additionally, a similar relationship was observed for a logged discount rate geometrically-averaged over the three reward sizes ($r = -0.535$, $p < 0.05$, Figure 1D). In other words, subjects with low sAA levels were more impulsive in intertemporal choice.

Discussion

Relationship between impulsive choice and testosterone

To our knowledge, this study is the first to demonstrate the existence of negative relationships between sAA levels and delay discounting of gains. Our results suggest

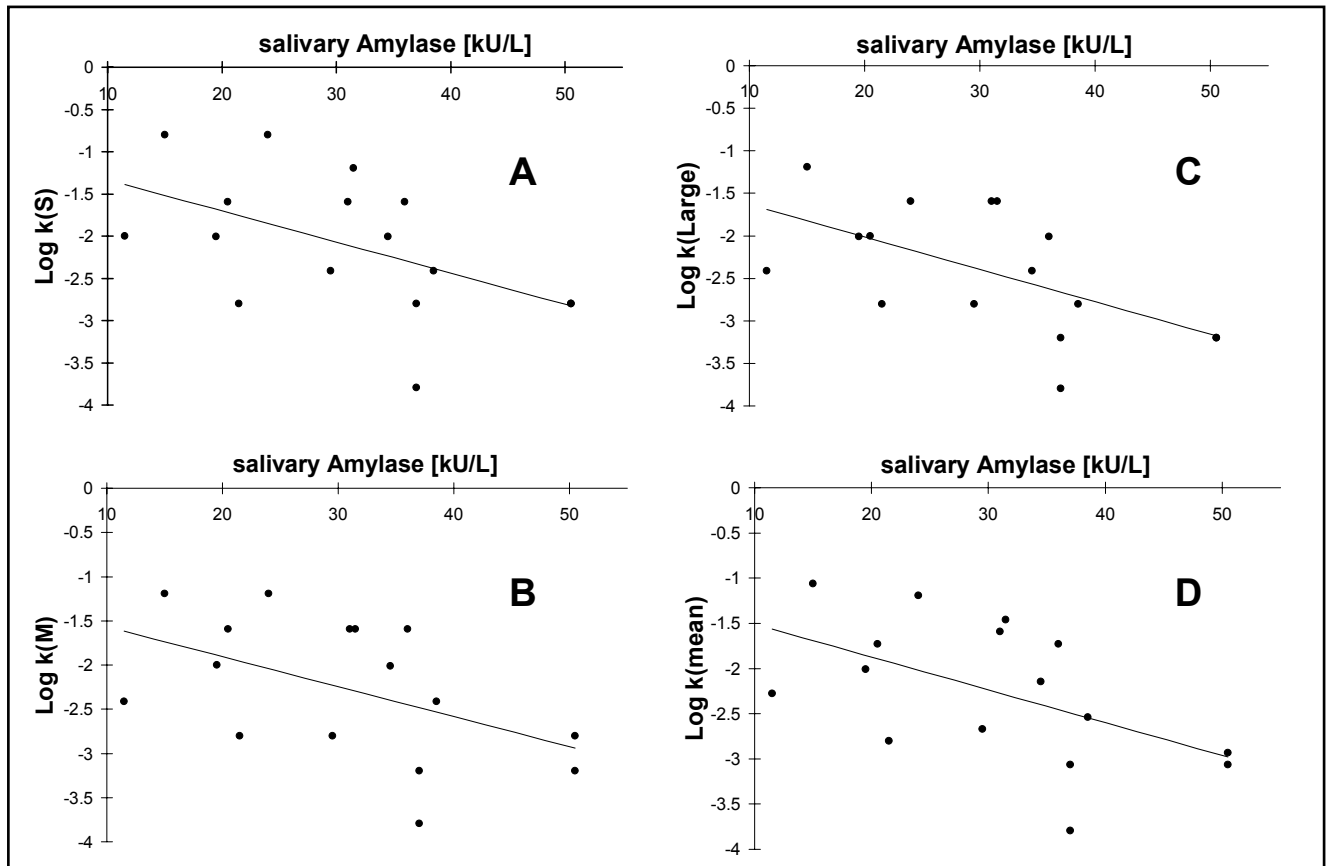


Figure 1. Scatterplots of sAA [kU/L] (horizontal axis) and discounting rates of delayed gains (vertical axis). Significant negative relations were observed ($p < 0.05$, for all coefficients). Note that large k corresponds to steep discounting (i.e., impulsivity in intertemporal choice).

that subjects with low SAM activities (as indicated with low sAA) are more impulsive in intertemporal choice, although serotonergic and dopaminergic contributions to self-control in intertemporal choice have been reported by neuropsychopharmacological studies in both rodents and humans [6,7,9,17].

Recent findings suggest that enhanced sAA levels may be associated with hyper-activation of beta-adrenergic pathways [15]. Consistent with our findings, it has been reported that pharmacological blockade of beta-adrenergic pathways (e.g. alpha2 receptors in the prefrontal cortex), which may have reduced sAA, dramatically enhanced ADHD-like symptoms such as impulsivity in monkeys [1]. Collectively, it can be speculated that sAA may, at least partially, reflect self control-related neurochemical activities (e.g., noradrenergic and dopaminergic activities) in the prefrontal cortex. This possibility should be examined in future studies combining sAA measurement and assessment of prefrontal functions with ERP/fMRI during performing intertemporal choice and/or tasks requiring self-control (e.g. error correction and detection). Moreover, considered that sAA and cortisol are both associated with anxious arousal [15,16], our present findings are also in line with previous reports: subjects with low cortisol levels are more impulsive in intertemporal choice [11] and risk-seeking in decision under uncertainty with possible negative outcomes (assessed with the IOWA gambling task [14]). However, neurobiological basis of sAA-arousal relationships are still unclear and future investigations should try to clarify these points.

Furthermore, neuropsychopharmacological studies reported that beta-adrenergic pathways play pivotal roles in decision-making under uncertainty with possible negative outcomes; namely, beta-blockade reduced the discrimination between large and small possible losses when the probability of winning was relatively low and the probability of losing was high [10]. To date, little has been investigated regarding the relationship between sAA and risky decision/ loss-aversion in probabilistic choice. Therefore, these relationships should be studied in order to further elucidate the roles of adrenergic and SAM systems in self-control in decision-making and behavior.

We now discuss limitations of our present study. We employed only male subjects in the present study. Because it is possible there is a gender difference in the relationships between sAA and impulsivity in intertemporal choice, females' sAA-discount rate relationships must be examined. Also, in the present study, we only assessed sAA. The following studies should examine the roles of sAA in impulsivity in relation to chronic cortisol levels and psychosocial stress-induced cortisol elevation.

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